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Impact of Different Methods of Synthesizing Starch Nanoparticles on the Percentage of Drug Loading

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ABSTRACT

Introduction: Finding a cost-effective drug with low side effects is crucial for cancer, as a significant burden on the healthcare system and patients. Despite numerous medications for cancer, low bioavailability and high toxicity limit their use. Starch, widely used in pharmaceutical industries, is one of the chosen carriers. This study utilizes SN38, a more potent metabolite of irinotecan and explores various methods for synthesizing starch nanoparticles.

Methods and Materials: The nanoprecipitation method utilizes a two-phase system, an organic phase (drug solvent), and an aqueous phase (starch solvent). Adding the organic phase to the aqueous phase forms a sediment of the drug surrounded by the starch. Herein, the organic phase was DMSO, while the aqueous phases included methanol, ethanol, acetonitrile, and dichloromethane. SN38 (1 mg) was dissolved in DMSO and added to the aqueous phase containing 10 mg of starch. The resulting sample was centrifuged at 11,000 rpm for 10 minutes to separate nanoparticles. In the emulsification technique, an oil phase of 10 mg of starch and 1 mg of SN38 in DMSO was added to water at 60 °C under sonication, creating an oil-in-water emulsion. Starch concentration in the oil phase varied (7.5, 10, 50, and 100 mg/ml). The particle size and polydispersity index (PI) were determined using dynamic light scattering. The drug loading amount was assessed with an ELISA reader at 383 nm, specific for SN38. Nanoparticle formation was confirmed through differential scanning calorimetry and infrared spectroscopy analysis.

Results: In the nanoprecipitation method, samples obtained from dichloromethane were disregarded as the presence of visible particles precluded their further consideration. Using methanol and ethanol resulted in nanoparticles with a PI ≥ 0.9 and particle sizes ranging from 300-400 nm. Acetonitrile-obtained particles had sizes between 200-300 nm and a PI ≤ 0.2; nonetheless, the drug loading in the nanoparticles did not surpass 10% in any sample. In the emulsification method, the optimal condition was 10 mg of starch with 1 mg of SN38. This combination resulted in a size range between 250 to 300 nm, an average PI of 0.5, and a drug loading efficiency of 92%. Further analysis through Fourier-transform infrared spectroscopy and dynamic state estimation techniques revealed the formation of two hydrogen bonds between the starch and SN38 molecules.

Conclusion and Discussion: The nanoprecipitation method, presents challenges with highly polar solvents like dichloromethane. The rapid changes in polarity and subsequent precipitation of starch can cause an undesirable increase in particle size. Also, this method can be unsuitable because of the hydrophobic nature of the drug and the rapid formation of precipitates. In contrast, the sonication method shows promise, as transforming starch into a gel state facilitates better drug entrapment in starch. However, further studies are needed to optimize the particle size and PI.

Keywords: Fourier-transform infrared spectroscopy, Nanoparticles, Starch

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